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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FALK, ANNE MARIE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/040,518	KARATZAS ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24,27-36,39-41 and 44-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24, 27-36, 39-41, and 44-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed March 9, 2005 has been entered. Claims 22 and 39 have been amended. Claims 25, 26, 42, and 43 have been cancelled.

Accordingly, Claims 22-24, 27-36, 39-41, and 44-58 remain pending in the instant application.

The remarks filed November 3, 2004 (hereinafter referred to as "the response") are considered herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 22-24, 27-36, 39-41, and 44-58 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record set forth in the Office Action of 5/3/2004. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants are referred to the final guidelines on written description published January 5, 2001 in the Federal Register at Volume 66, Number 4, pp. 1099-1111 (also available at www.uspto.gov).

At page 7 of the response, Applicants assert that this rejection is obviated by the amendment to Claim 22. Applicants further state that the Patent Office acknowledges that the particular biofilament polypeptides from the two spider species recited in Claim 22 permit construction of a nucleic acid construct as claimed. However, while Applicants seem to suggest that the claim is limited to these

biofilament polypeptides (presumably referring to dragline silk polypeptides of *Nephila clavipes* or *Araneus diadematus*), the claim language is not so limiting. The claim has been amended to add the phrase "wherein said biofilament polypeptide comprises a plurality of repeat motifs as present in dragline silk produced by *Nephila clavipes* or *Araneus diadematus*." Thus, the claim language does not limit the biofilament polypeptide to dragline silk proteins produced by *Nephila clavipes* or *Araneus diadematus*. Rather, the claims only require that the biofilament polypeptide comprises a plurality of repeat motifs "as present in dragline silk produced by *Nephila clavipes* or *Araneus diadematus*." Given its broadest reasonable interpretation this claim language merely points to an exemplary polypeptide that comprises a plurality of repeat motifs, and is therefore non-limiting claim language. See the rejection under 35 U.S.C. 112, second paragraph set forth below. Thus, contrary to Applicants' assertion, the claims are not limited to nucleic acids encoding dragline silk protein from the two spider species recited in Claim 22.

Thus, the rejection is maintained for reasons of record.

With regard to the written description rejection of Claims 39, 40, and 44-53, the rejection is maintained for failing to describe the entire genus of nucleic acid molecules encompassed by the claims. However, the written description rejection with regard to the genus of transgenic ruminants encompassed by the claims is withdrawn in view of the amendment to Claim 39 which now recites "a transgenic female ruminant comprising germline and somatic cells that comprise the nucleic acid molecule of claim 22, wherein the ruminant secretes a biofilament polypeptide into the milk."

At page 8, paragraph 2 of the response, Applicants assert that the rejection is obviated in view of the amendment to Claim 39. Applicants further submit that the written description requirement is met with respect to Claims 39, 40, and 44-53. On the contrary, the claims continue to encompass the use of nucleic acid molecules that are not described in the specification. Claims 39, 40, and 44-53 depend from Claim 22, which is directed to a genus of nucleic acid molecules not described by the instant specification. As set forth in the Office Action of 5/3/2004, "only 6 biofilament polypeptides from 2

species of spiders out of 34,000 species have been described in sufficient detail to permit construction of a nucleic acid construct as claimed" (Office Action at page 3).

Enablement

Claims 22-36, 39, 40, 44-53, and 54-58 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

(i) a nucleic acid molecule comprising a mouse whey acidic protein (WAP) promoter operably linked to a nucleotide sequence encoding a polypeptide, wherein said polypeptide comprises a biofilament polypeptide and a leader sequence that enables secretion of said biofilament polypeptide by milk-producing cells into milk of a ruminant, and wherein said biofilament polypeptide is a dragline silk polypeptide produced by *Nephila clavipes* or *Araneus diadematus*; and

(ii) a transgenic female ruminant comprising germline and somatic cells that comprise the nucleic acid molecule as set forth in part (i), wherein the ruminant secretes a biofilament polypeptide into milk; and

(iii) a method for producing a biofilament polypeptide, comprising: providing a transgenic female ruminant of part (ii) and isolating the biofilament polypeptide from milk produced by the transgenic female ruminant,

does not reasonably provide enablement for the full scope of the claimed inventions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Declaration of Dr. Karatzas, filed December 3, 2004, has been fully considered and is found to be partially persuasive. The Declaration states that the methods described in the specification were used to generate founder goats by pronuclear microinjection and that the goats were transgenic for the ADF-3 gene under control of the WAP promoter and leader sequences as described in the '518

application. The Declaration further states that seven female transgenic progeny of goats generated by pronuclear microinjection were obtained that expressed 20-400 milligrams of MaSpI per liter of milk and that the MaSpI gene was under control of the WAP promoter. Although it is unclear which leader sequence was used to arrive at the result described in the Declaration, Applicants' statement, that the leader sequence is one of those described in the '518 application (Declaration at paragraph 6), is relied upon in defining the scope of enablement indicated hereinabove.

At page 8, paragraph 5 of the response, Applicants assert that the Declaration of Dr. Karatzas, filed April 18, 2002, provides evidence that the biofilament polypeptides can and do express in milk-producing cells of a ruminant and that such polypeptides are secreted into the milk of the transgenic ruminant. Applicants further assert that paragraphs 4a to 4c of that Declaration describes transgenic goats comprising a nucleic acid encoding the ADF-3, MaSpI (referred to as NcDS-1 in the specification), or MaSpII (allegedly referred to as NcDS-2 in the specification) biofilament polypeptides under control of the WAP promoter expressed biofilament polypeptide in their milk. Applicants further assert that paragraph 4c of that Declaration states that "some [goats] made more than 1 gram of MaSpII protein per liter of milk." This Declaration has already been fully addressed in the Office Action of 5/3/2004. As noted therein, the MaSpII transgenic goats were generated by nuclear transfer, a method not disclosed or contemplated in the instant specification. The instant specification only discloses using pronuclear microinjection to generate transgenic ruminants. Thus, the MaSpII experiments described in the Declaration were not performed in accordance with the teachings of the specification. With regard to the ADF-3 transgenic goats and MaSpI transgenic goats, it was noted in the Office Action of 5/3/2004 that the Declaration does not report the quantity of biofilament protein present in the milk (Office Action at page 6, paragraph 5).

At page 9, paragraph 1 of the response, Applicants assert that the Patent Office is factually incorrect to assert that the nucleic acids recited in the claims, the transgenic female ruminant, or the

methods claimed, "do not work for lack of expression, since the biofilament polypeptides recited in amended Claim 22 clearly can be expressed in milk." Contrary to Applicants' statement, no such assertion has been made by the Patent Office. Rather, the rejection states that since the asserted utility of the animal is for isolation of the biofilament protein from the milk, the specification must provide an enabling disclosure for producing sufficient quantities of biofilament protein to permit isolation from the milk (Office Action of 5/3/2004 at page 6, paragraph 5).

At page 9, paragraph 2 of the response, Applicants assert that the ADF-3 and MaSpI polypeptides expressed in the milk of the transgenic goats referred to in the Declaration of April 18, 2002 were identified in the milk by Western blot and molecular weight measurement. Applicants state that "given that these techniques require the target protein to be isolated from other non-target protein, suggests that, in fact, ADF-3 and MaSpI are expressed in quantities sufficient to permit their isolation." First, it is noted that "molecular weight measurement" is not a technique itself. Rather, "molecular weight measurement" of a protein can be performed by a variety of techniques known in the art, but the Declaration does not elucidate which technique was used. Thus, there is no evidence presented in the Declaration to suggest that "ADF-3 and MaSpI are expressed in quantities sufficient to permit their isolation" as Applicants now contend. Second, it is noted that Western blot does not require isolation of a target protein from other non-target proteins, as Applicants now contend. On the contrary, the technique requires the use of **specific antibodies** to detect the target protein from a sample of impure protein extract precisely due to the fact that the sample applied to the gel is an impure extract. Thus, the use of Western blot to detect a protein does not in any way suggest that the protein of interest is isolated from non-target proteins, as Applicants contend.

In view of the Declaration of December 3, 2004, the specification provides enablement for the scope indicated hereinabove, but fails to provide an enabling disclosure over the full scope for reasons of record set forth in the Office Action of 5/3/2004.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24, 27-36, 39-41, and 44-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is indefinite in its recitation of "a plurality of repeat motifs as present in dragline silk produced by *Nephila clavipes* or *Araneus diadematus*" because it is unclear how much similarity is required to be present between the repeat motifs present in the claimed nucleic acid and the repeat motifs present in *Nephila clavipes* or *Araneus diadematus* dragline silk. Are the repeat motifs in *Nephila clavipes* and *Araneus diadematus* dragline silk simply examples of repeat motifs? If so, then will any type of repeat motif satisfy this claim limitation? Do the "plurality of repeat motifs" have to be identical to the repeat motifs present in *N. clavipes* or *A. diadematus* dragline silk? Or can the "plurality of repeat motifs" be somewhat similar to the repeat motifs present in *N. clavipes* or *A. diadematus* dragline silk? If so, how similar do the repeat motifs have to be? The phrase "as present in" constitutes a relative term that is not defined in the instant specification. Claims 23, 24, 27-36, 39-41, and 44-58 are indefinite insofar as they depend from Claim 22.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22-24, 27-36, 41, 44-53, and 54-58 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Huynh et al. (1991, Experimental Cell Research 197: 191-199), U.S. Patent No. 5,227,301 (Turner et al., 1993), Fahnestock et al. (1997, Appl. Microbiol. Biotechnol. 47: 23-32), and Ebert et al. (1994, Bio/Technology 12: 699-702), for reasons of record set forth in the Office Action of 5/3/2004.

Claims 41 and 44-53 are directed to a method for producing a biofilament polypeptide by culturing a mammary epithelial cell comprising a nucleic acid construct, under conditions in which said biofilament polypeptide is expressed and secreted into a culture medium. The nucleic acid construct comprises a nucleic acid encoding a biofilament polypeptide operably linked to a regulatory sequence that directs expression of a polypeptide in milk-producing cells of a ruminant, wherein said biofilament polypeptide comprises a leader sequence that enables secretion of said biofilament polypeptide by said milk producing cells into milk of the ruminant.

Claims 22-24, 27-36 and 54-58 are directed to nucleic acid molecules.

Huynh et al. (1991) and Turner et al. (1993) disclose a clonal cell line produced from primary bovine mammary alveolar cells (MAC-T) by stable transfection with a vector encoding SV40 large T antigen. The immortalized cells do not exhibit a transformed phenotype. The cells are responsive to lactogenic hormones (p. 198, column 2 of Huynh et al.). When differentiated, the cells synthesize and secrete α- and β-casein. Thus, the phenotype of the cells makes them suitable as an *in vitro* model for bovine lactation. Turner et al. explicitly points out that the cell line can be used in a method for indefinitely expressing foreign genes (see abstract and Example III at Column 10). Turner et al. also points out that eukaryotic fermentation is a viable means of overcoming the considerable problems associated with prokaryotic expression (column 10), since eukaryotic proteins require posttranslational modification and the proper folding environment (column 10).

Fahnestock et al. (1997) disclose the production of synthetic spider dragline silk proteins in *Escherichia coli*. The expression system is not ideal for expressing eukaryotic proteins, as acknowledged at page 30, column 2, paragraph 5. The experiments performed revealed a number of difficulties associated with expression of the synthetic spidroin genes, including truncated synthesis, poor codon adaptation, and genetic instability. The authors further noted that the spidroin-1 and spidroin-2 genes are highly repetitive at the DNA level and are both poorly adapted to expression in *E. coli*.

Ebert et al. (1994) disclose the production of a human recombinant protein in the milk of transgenic goats. The human cDNA was inserted between exons 2 and 7 of the goat β-casein gene. Lactation was induced and milk containing the human recombinant protein was harvested.

Since spider silk proteins have desirable properties, such as high tensile strength and elasticity, skilled artisans are clearly interested in producing these proteins in large quantities, as evidenced by the work of Fahnestock et al. Since the cell line disclosed by Huynh et al. has been shown to synthesize and secrete milk proteins into culture media, one of skill in the art would recognize that the cells disclosed by Huynh et al. (1991) are ideal for expressing recombinant proteins that will be secreted directly into the culture media, which would clearly facilitate isolation of the recombinant protein. Moreover, given the problems revealed in attempting to express synthetic spider dragline silk proteins in *E. coli*, one of skill in the art would have realized that a eukaryotic expression system would be more compatible for expression of eukaryotic genes. In view of the successful expression of human tissue plasminogen activator in the mammary gland of transgenic goats, the skilled artisan would have readily recognized the advantages of expressing silk proteins in mammary epithelial cells in culture. Thus, it would have been obvious to one of skill in the art to have used a β-casein construct analogous to that depicted in Figure 1 of Ebert et al. for insertion of the *Nephila clavipes* synthetic genes described by Fahnestock et al. The resulting construct would be used to transfect the mammary epithelial cell line of Huynh et al. One of skill in the art would have anticipated a reasonable expectation of success because the desired cell line was readily

available and had already been shown to have the necessary phenotype, *i.e.* it is responsive to lactogenic hormones and secretes milk proteins.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

At page 10 of the response, Applicants assert that neither Huynh et al. nor Turner et al. teach or suggest "a nucleic acid molecule comprising [sic] a biofilament polypeptide and a leader sequence that enables secretion of said biofilament polypeptide by said milk-producing cells into milk of the ruminant, and wherein said biofilament polypeptide comprises a plurality of repeat motifs as present in dragline silk produced by *Nephila clavipes* or *Araneus diadematus*." In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Huynh et al. and Turner et al. need not teach or suggest a nucleic acid molecule encoding a biofilament polypeptide because the rejection is based on a combination of references that render the instantly claimed invention obvious. Huynh et al. and Turner et al. are cited for teaching a clonal cell line produced from primary bovine mammary alveolar cells (MAC-T). The cells are responsive to lactogenic hormones (p. 198, column 2 of Huynh et al.). When differentiated, the cells synthesize and secrete α- and β-casein. Thus, the phenotype of the cells makes them suitable as an *in vitro* model for bovine lactation. Turner et al. explicitly points out that the cell line can be used in a method for indefinitely expressing foreign genes (see abstract and Example III at Column 10). Turner et al. also points out that eukaryotic fermentation is a viable means of overcoming the considerable problems associated with prokaryotic expression (column 10), since eukaryotic proteins require posttranslational modification and the proper folding environment (column 10). Claim 3 is directed to expressing any foreign gene in the cell line, using a DNA construct

comprising a bovine casein promoter and the coding sequence from a foreign gene. The claim is directed to determining the suitability of the foreign DNA construct prior to making a transgenic bovine.

At page 11, paragraph 1 of the response, Applicants assert that Turner et al. fails to teach or suggest expressing spider silk biofilament polypeptides in the milk of a ruminant. Applicants are reminded that Claim 40 is not included in the rejection, and therefore Turner et al. need not teach or suggest expressing spider silk biofilament polypeptides in the milk of a ruminant.

At page 11, paragraph 2 of the response, Applicants assert that Fahnestock et al. does not teach or suggest "a nucleic acid molecule encoding spider silk polypeptides and a leader sequence that enables secretion of the biofilament polypeptide by milk-producing cells into milk of a ruminant, or a method of using the nucleic acid molecule to produce a biofilament polypeptide." In response to applicant's arguments against the references individually, Applicants are again reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Fahnestock et al. need not teach "a nucleic acid molecule encoding spider silk polypeptides and a leader sequence that enables secretion of the biofilament polypeptide by milk-producing cells" because Fahnestock et al. is cited for demonstrating that the *E. coli* expression system is inadequate for expressing spider silk proteins. The experiments performed revealed a number of difficulties associated with expression of the synthetic spidroin genes, including truncated synthesis, poor codon adaptation, and genetic instability (page 30, column 2, paragraph 5). The authors point out that both the spidroin-1 and spidroin-2 genes are poorly adapted to expression in *E. coli*. Given these teachings, one skilled in the art would look to eukaryotic expression systems for producing spider silk proteins.

At page 11, paragraph 2 of the response, Applicants further assert that Fahnestock et al. do not teach or suggest using alternative expression systems, but only provide ideas on how to express spider

silk proteins in *E. coli*. Nevertheless, the rejection does not rely on Fahnestock et al. for teaching an alternative expression system, but rather relies on Huynh et al. and Turner et al. for teaching an appropriate eukaryotic expression system as an alternative to expressing eukaryotic proteins in prokaryotic systems. Turner et al. provide the express teaching that problems associated with expressing eukaryotic proteins in prokaryotic expression systems can be overcome by using a eukaryotic expression system which will provide the appropriate post-translational modification and the proper folding environment to produce active protein (Column 10 of Turner et al.).

At page 11, paragraph 3 of the response, Applicants assert that "it is factually incorrect to characterize Fahnestock & Irwin as stating that the problems of expressing spider silk proteins in *E. coli* as a result of that prokaryotic expression system." The Examiner does not agree because the reference as a whole is itself a demonstration of the limitations of the *E. coli* expression system used. The authors recognized and reported on the limitations of such an expression system, stating, "[s]erious instability of the natural genes in *E. coli* has been described (Hinman et al. 1992)." While the authors suggested using synthetic genes to alleviate these difficulties, the skilled artisan would have readily recognized that the statements made by the authors point to the inadequacies of the *E. coli* expression system. Thus, the reference, when taken as a whole, suggests to the skilled artisan the need for an appropriate expression system for the production of spider silk proteins.

In the paragraph bridging pages 11-12 of the response, Applicants assert that Ebert et al. do not teach or suggest "a nucleic acid molecule encoding a spider silk biofilament polypeptide linked to a signal peptide for expression into milk, or methods of producing a biofilament polypeptide using such a nucleic acid." In response to applicant's arguments against the references individually, Applicants are again reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Ebert et al. need not teach or suggest

a nucleic acid encoding a spider silk protein linked to a signal peptide for expression into milk because Ebert et al. is cited for teaching the production of human recombinant tissue plasminogen activator in the milk of transgenic goats. The goat β-casein promoter was used to drive expression of the human protein. Lactation was induced and milk containing the human recombinant protein was harvested.

At page 12, paragraph 1 of the response, Applicants assert that the expression of hTPA in goat milk fails to suggest anything about the expression of biofilament polypeptides in milk. Applicants are again reminded that the rejection does not pertain to Claim 40, which is directed to producing a biofilament polypeptide in the milk of a transgenic ruminant. Rather, Ebert et al. is relied upon for teaching a DNA construct useful for generating a nucleic acid molecule encoding a spider silk protein fused to a leader sequence that enables secretion of the biofilament polypeptide by milk-producing cells, and further wherein the nucleic acid molecule comprises a regulatory sequence that directs expression of the polypeptide in milk-producing cells. As stated in the rejection, "it would have been obvious to one of skill in the art to have used a β-casein construct analogous to that depicted in Figure 1 of Ebert et al. for insertion of the *Nephila clavipes* synthetic genes described by Fahnestock et al." The rejection goes on to state that "[t]he resulting construct would be used to transfect the mammary epithelial cell line of Huynh et al. One of skill in the art would have anticipated a reasonable expectation of success because the desired cell line was readily available and had already been shown to have the necessary phenotype, *i.e.* it is responsive to lactogenic hormones and secretes milk proteins."

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER